

### **AMENDMENTS TO THE SPECIFICATION**

Please add at page 1, after the title, the following paragraph:

#### **CROSS-REFERENCE TO RELATED APPLICATIONS**

This application is the National Phase filing of International Patent Application No. PCT/JP03/06942, filed June 2, 2003, which claims priority to JP 2002-162206, filed June 3, 2002, and to JP 2002-255612, filed August 30, 2002.

Please replace the paragraph at page 39, line 21 to page 40, line 3 with the following paragraph:

Additives miscible with tablets, capsules, etc. include a binder such as gelatin, corn starch, tragacanth and gum arabic, an excipient such as crystalline cellulose, a swelling agent such as corn starch, gelatin and alginic acid, a lubricant such as magnesium stearate, a sweetening agent such as sucrose, lactose and saccharin, and a flavoring agent such as peppermint, akamono oil and cherry. When the unit dosage is in the form of capsules, liquid carriers such as oils and fats may further be used together with the additives described above. A sterile composition for injection may be formulated by conventional procedures used to make pharmaceutical compositions, e.g., by dissolving or suspending the active ingredients in a vehicle such as water for injection with a naturally occurring vegetable oil such as sesame oil and coconut oil, etc. to prepare the pharmaceutical composition. Examples of an aqueous medium for injection include physiological saline and an isotonic solution containing glucose and other auxiliary agents (e.g., D-sorbitol, D-mannitol, sodium chloride, etc.) and may be used in combination with an appropriate dissolution aid such as an alcohol (e.g., ethanol), a polyalcohol (e.g., propylene glycol and polyethylene glycol), a nonionic surfactant (e.g., Polysorbate ~~polyserbate~~ 80<sup>TM</sup> and HCO-50), etc. Examples of the oily medium include sesame oil and soybean oil, which may also be used in combination with a dissolution aid such as benzyl benzoate and benzyl alcohol.

Please replace the paragraph at page 41, line 33 to page 42, line 5 with the following paragraph:

(i) A non-human mammal (e.g., mouse, rat, rabbit, sheep, swine, bovine, cat, dog, monkey and the like) having cells that express a normal AR or the mutant AR of the present invention receive administration of a drug or physical stress, and blood, specific organs, or tissues or cells isolated from the organs are obtained after a specified period of time. The mRNA encoding the mutant AR of the present invention contained in the thus obtained cells is

extracted from the cells, for example, in a conventional manner and quantified using, e.g., TaqMan<sup>TM</sup>-PCR, or may also be analyzed by Northern blot technique by publicly known methods.

Please replace the paragraph at page 44, line 24 to page 45, line 6 with the following paragraph:

Additives miscible with tablets, capsules, etc. include a binder such as gelatin, corn starch, tragacanth and gum arabic, an excipient such as crystalline cellulose, a swelling agent such as corn starch, gelatin and alginic acid, a lubricant such as magnesium stearate, a sweetening agent such as sucrose, lactose and saccharin, and a flavoring agent such as peppermint, akamono oil and cherry. When the unit dosage is in the form of capsules, liquid carriers such as oils and fats may further be used together with the additives described above. A sterile composition for injection may be formulated by conventional procedures used to make pharmaceutical compositions, e.g., by dissolving or suspending the active ingredients in a vehicle such as water for injection with a naturally occurring vegetable oil such as sesame oil and coconut oil, etc. to prepare the pharmaceutical composition. Examples of an aqueous medium for injection include physiological saline and an isotonic solution containing glucose and other auxiliary agents (e.g., D-sorbitol, D-mannitol, sodium chloride, etc.) and may be used in combination with an appropriate dissolution aid such as an alcohol (e.g., ethanol), a polyalcohol (e.g., propylene glycol and polyethylene glycol), a nonionic surfactant (e.g., Polysorbate 80<sup>TM</sup> and HCO-50), etc. Examples of the oily medium include sesame oil and soybean oil, which may also be used in combination with a dissolution aid such as benzyl benzoate and benzyl alcohol.

Please replace the paragraph at page 53, line 28 to page 54, line 10 with the following paragraph:

Additives miscible with tablets, capsules, etc. include a binder such as gelatin, corn starch, tragacanth and gum arabic, an excipient such as crystalline cellulose, a swelling agent such as corn starch, gelatin and alginic acid, a lubricant such as magnesium stearate, a sweetening agent such as sucrose, lactose and saccharin, and a flavoring agent such as peppermint, akamono oil and cherry. When the unit dosage is in the form of capsules, liquid carriers such as oils and fats may further be used together with the additives described above. A sterile composition for injection may be formulated by conventional procedures used to make pharmaceutical compositions, e.g., by dissolving or suspending the active ingredients in a vehicle such as water for injection with a naturally occurring vegetable oil such as sesame oil and coconut oil, etc. to prepare the pharmaceutical composition. Examples of an aqueous medium for injection include physiological saline and an isotonic solution containing

glucose and other auxiliary agents (e.g., D-sorbitol, D-mannitol, sodium chloride, etc.) and may be used in combination with an appropriate dissolution aid such as an alcohol (e.g., ethanol), a polyalcohol (e.g., propylene glycol and polyethylene glycol), a nonionic surfactant (e.g., Polysorbate ~~polysorbate~~ 80<sup>TM</sup> and HCO-50), etc. Examples of the oily medium include sesame oil and soybean oil, which may also be used in combination with a dissolution aid such as benzyl benzoate and benzyl alcohol.

Please replace the paragraph at page 59, line 20 to page 60, line 1 with the following paragraph:

As examples of the composition for parenteral administration, injections, suppositories and the like are used; the injections include dosage forms such as intravenous injections, subcutaneous injections, intracutaneous injections, intramuscular injections and drip infusion injections. Such an injection is prepared according to a publicly known method, for example, by dissolving, suspending or emulsifying the above-described antibody or a salt thereof in a sterile aqueous or oily solution normally used for injections. As examples of aqueous solutions for injection, physiological saline, an isotonic solution containing glucose or another auxiliary drug, and the like can be used, which may be used in combination with an appropriate solubilizer, for example, alcohol (e.g., ethanol), polyalcohol (e.g., propylene glycol, polyethylene glycol), non-ionic surfactant [e.g., Polysorbate ~~polysorbate~~ 80<sup>TM</sup>, HCO-50 (polyoxyethylene (50 mol) adduct of hydrogenated castor oil)] and the like. As examples of oily solutions, sesame oil, soybean oil and the like can be used, which may be used in combination with benzyl benzoate, benzyl alcohol and the like as solubilizers. The prepared injection solution is normally filled in an appropriate ampoule. Suppositories used for rectal administration are prepared by mixing the above-described antibody or a salt thereof in an ordinary suppository base.

Please replace the paragraph at page 79, line 29 to page 80, line 15 with the following paragraph:

After genomic DNA was extracted from LNCaP-FGC cells according to a conventional method, a PCR reaction was conducted with this as the template using 5'-GGAGCTCGAATTCACATTGTTTGCTGCACGTTGG-3' (SEQ ID NO: 5) and 5'-CAAGCTTTGGGGCTGGGGAGCCTCCCCAGGAGC-3' (SEQ ID NO: 6) as the primers. Using Pyrobest<sup>TM</sup> (TaKaRa) as the DNA polymerase, the PCR reaction was conducted in 25 cycles of heating at 94°C for 1 minute, followed by heating at 98°C for 5 seconds, at 59°C for 30 seconds, and at 72°C for 1 minute, with the ~~GeneAmp~~ GeneAmp<sup>TM</sup> PCR System 9700 (Applied Biosystems), to yield an about 650 bp DNA fragment containing the PSA

(prostate-specific antigen) promoter. After this fragment was cleaved with restriction endonucleases Hind III (TaKaRa) and Sac I (TaKaRa), it was subjected to agarose gel electrophoresis, and a DNA fragment was recovered. The DNA fragment was mixed with the pGL3-Basic vector (Promega), previously digested with Hind III and Sac I, and ligated using the Ligation high (TOYOBO), and *Escherichia coli* DH5 $\alpha$ <sup>TM</sup> competent cells were transformed, to yield the vector pGL3-PSA-Luc, which has the luciferase gene ligated downstream of the PSA promoter. Furthermore, after pGL3-PSA-Luc was cleaved with Hind III, blunting was conducted using a Blunting kit (TaKaRa), after which the blunt-ended fragment was cleaved with Kpn I (TaKaRa) and a fragment containing the PSA promoter was recovered. After the DNA fragment was cleaved with Sac I, blunting was conducted using a Blunting kit, and the blunt-ended fragment was ligated to Kpn I-cleaved pGL3-PSA-Luc, and *Escherichia coli* DH5 $\alpha$ <sup>TM</sup> competent cells were transformed, to yield pGL3-2PSA-Luc, which has two PSA promoters ligated tandem.

Please replace the paragraph at page 80, lines 18-26 with the following paragraph:

5,000,000 cells of Cos-7 were sown to a 150 cm<sup>2</sup> flask and cultured in a culture broth (DMEM+10% Dextran Charcoal (DCC)-Fetal Bovine Serum (FBS)+2 mM glutamine) for 24 hours, after which pGL3-PSA-Luc or pGL3-2PSA-Luc obtained in Reference Example 1 above and a vector DNA incorporating a wild type AR were co-transfected using SuperFect<sup>TM</sup> (Qiagen). Two hours later, the medium was replaced with a fresh one and 3 hours of cultivation was conducted, after which 1  $\mu$ M DHT (5 $\alpha$ -dihydrotestosterone) was added and further 24 hours of cultivation was conducted, after which luciferase activity was measured and transcription activity was examined. The results are shown in FIG. 5.